REMARKS

Claims 1-45 are pending. Claims 27-43 are withdrawn from consideration. Claims 1-26, 44, and 45 stand rejected. Applicants amend claims 44 and 45. Accordingly, after entry of this Amendment, claims 1-26, 44, and 45 will be pending for examination. Applicants submit that the amendments introduce no new matter and that claims 1-26, 44, and 45 are in condition for allowance.

Amendments to the Claims

Applicants amend claims 44 and 45 to clarify the route of administration of the fusion proteins of the invention. Support for the amendments is found in the application as filed at least at page 28, line 26 to page 29, line 5. Accordingly, Applicants submit that no new matter is introduced by these amendments.

Restriction Requirement

Applicants affirm the election with traverse to prosecute the invention of Group I, i.e., claims 1-26, 44, and 45.

Claim Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 11-13, 24, and 25 are rejected under 35 U.S.C. § 112, first paragraph, because, although the specification is enabling for IL-2, CMCSF, IL-4R, and FLT-3L as adjuvants, the specification allegedly does not reasonably provide enablement for "all other" cytokines as adjuvants in a method of enhancing the immunogenicity of a preselected antigen.

The proper standard of enablement under 35 U.S.C. § 112, first paragraph, is whether one skilled in the art could make and use the invention without undue experimentation based on the disclosure in the patent application coupled with information known in the art. This standard does not require an applicant to describe in an application every conceivable embodiment of the invention. Rather, the enablement requirement is met when there is a reasonable belief that applicant's success with one embodiment of the invention could be extrapolated to other embodiments by one skilled in the art at the time of the invention.

Applicants submit that the specification contains teachings of the manner and process of making and using the invention in terms that correspond in scope to those used in describing and defining the subject matter sought to be patented. Specifically, as the Office action admits, the specification provides enablement for a number of cytokines that are encompassed by the generic description. Further, cytokines are a limited class of molecules which are understood in the art to be a group of proteins produced during the effector phases of natural and specific immunity and serve to mediate and regulate immune and inflammatory responses. See, e.g., Chapter 11, "Cytokines" in Abbas A.K., et al., *Cellular and Molecular Immunology*, pp. 225-243 (W.B. Saunders Company, 1991). Moreover, cytokine actions are often redundant, with many functions being the shared amongst different cytokines. See Id. Accordingly, cytokines other than those specifically enabled within the specification would be expected to be useful in the practice of the invention.

With respect to undue experimentation to prepare fusion proteins containing an adjuvant of the invention which includes a cytokine, Applicants submit that the specification and knowledge of one of ordinary skill in the art provide the necessary teachings to enable one to make and use the fusion proteins containing an adjuvant without undue experimentation. Methods and techniques in cellular and molecular biology and immunology have advanced such that a skilled artisan can routinely make functional fusion proteins composed of a variety of protein and/or peptide fragments. Accordingly, based on the teachings of the specification and the knowledge in the art, a skilled artisan would be able to prepare a fusion protein of the invention containing an adjuvant without undue experimentation. Subsequently, a skilled artisan readily would be able to determine whether the fusion protein containing the cytokine would be useful in practicing the invention.

Accordingly, based on the remarks presented above, Applicants respectfully request reconsideration and withdrawal of this rejection.

Claim Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 44 and 45 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Office action asserts that it is unclear as to what is meant by the term "localizing protein."

Applicants submit that "localizing protein" is definite and would be understood by a skilled artisan. Specifically, as taught in the specification, a localizing protein is a protein that enhances the delivery to, or processing by, an antigen presentation system, i.e., the antigen processing and presentation machinery of the immune system. See application as filed, page 7, lines 21-30. An Fc moiety is an example of a localizing protein. See application as filed, page 8, line 5. Accordingly, Applicants submit that the term "localizing protein" is definite to one of ordinary skill in the art and respectfully request reconsideration and withdrawal of this rejection.

Claim Rejections Under 35 U.S.C. § 103

Claims 1-26, 44, and 45 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Harvill et al., *J. Immunol.*, 157: 3165-3170 (1996) ("Harvill") in view of U.S. Patent No. 5,349,053 to Landolfi ("Landolfi").

To render a claimed invention obvious, a combination of prior art references must teach or suggest all the claim limitations. Harvill and Landolfi fail to teach or suggest each of the limitations in independent claims 1, 15, 44, and 45. Specifically, with respect to claims 1 and 15, Harvill and Landolfi fail to teach or suggest a fusion protein which includes an immunoglobulin heavy chain constant region and an antigen. With respect to claims 44 and 45, Harvill and Landolfi fail to teach or suggest a fusion protein which includes a localizing protein and an antigen.

Harvill teaches an anti-DNS-IgG3-IL-2 construct. Harvill further teaches that an antigen can be associated with this construct by linking the antigen to a hapten dansyl (DNS). See Harvill, p. 3169, col. 2, lns. 7-19. However, the resulting associated complex is not a fusion protein which includes an immunoglobulin heavy chain constant region and an antigen, or a

localizing protein and an antigen. Rather, the complex of Harvill is an association of an antigen with an IgG3 molecule using DNS, a non-protein chemical compound. Accordingly, Harvill does not teach each limitation of each of independent claims 1, 15, 44, and 45.

Landolfi does not cure the deficiency of Harvill. That is, Landolfi does not teach or suggest a fusion protein which includes an immunoglobulin heavy chain constant region and an antigen, or a localizing protein and an antigen. Accordingly, considered as a whole, Applicants' claimed invention recited in independent claims 1, 15, 44, and 45 is unobvious over Harvill in view of Landolfi at least because the combination of references fails to teach or suggest each limitation of claim 1, 15, 44, or 45. Therefore, Applicants respectfully request reconsideration and withdrawal of this rejection.

In addition, Landolfi teaches away from Applicants claimed invention. Specifically, Landolfi teaches "immunoligands" where the variable region of an immunoglobulin is replaced, or substantially replaced, with a ligand component which provides the immunoligand with its binding specificity. See Landolfi, col. 4, lns. 15-19. "Despite conjugation to the ligand binding component, the normal effector function of the immunoglobulin constant region component may be retained." Landolfi, col. 4, lns. 28-30. Thus, the effector functions of the immunoglobulin constant regions are maintained while the variable region is modified to provide binding specificity.

In Applicants' claimed invention, the immunoglobulin heavy chain constant region, which is an example of a localizing protein, provides the binding specificity for the fusion protein. Accordingly, Landolfi teaches away from Applicants' claimed invention because Landolfi exploits the effector functions of the immunoglobulin constant regions, not their binding specificity. Thus, a skilled artisan reading Landolfi would not be motivated to make and practice that which Applicants claim. Therefore, Applicants submit that the invention recited in claims 1, 15, 44, and 45 is unobvious in view of the teachings of Landolfi, and respectfully request that this rejection be reconsidered and withdrawn.

Applicants submit that claims 1, 15, 44, and 45 are novel and unobvious over the cited references, either alone or in combination. Because claims 2-14 and 16-26 depend directly or indirectly from claims 1 and 15, respectively, Applicants also submit that claims 2-14 and 16-26 are patentable over the cited references.

CONCLUSION

Based on the above amendments and remarks, Applicants respectfully submit that pending claims 1-26, 44, and 45 are in condition for allowance and request entry as such. If the Examiner believes that a conversation with Applicant's attorney would be helpful in expediting prosecution of this application, the Examiner is invited to contact the undersigned.

Respectfully submitted,

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MARKED UP VERSION OF AMENDED CLAIMS SHOWING AMENDMENTS

44. (Amended) A method for enhancing the immunogenicity of a preselected antigen in a mammal, the method comprising:

administering to a mammal intramuscularly, intravenously, transdermally or subcutaneously, either simultaneously or sequentially, a first fusion protein comprising an antigen protein with a localizing protein, and a second fusion protein comprising an adjuvant protein and said localizing protein, said localizing protein causing an increase in concentration of said first and second fusion proteins in a region of the mammal accessible to the immune system.

45. (Amended) A method for enhancing the immunogenicity of a preselected antigen in a mammal, the method comprising:

administering to a mammal intramuscularly, intravenously, transdermally or subcutaneously, a fusion protein comprising an antigen protein, an adjuvant protein and a localizing protein, said localizing protein causing an increase in concentration of said antigen and adjuvant proteins in a region of the mammal accessible to the immune system.